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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BROOKS, KRISTIE LATRICE	
ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/758,241	SUNDERMANN ET AL.	
	Examiner	Art Unit	
	KRISTIE L. BROOKS	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *1-38 and 43-53* is/are allowed.

6)☒ Claim(s) *39-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-53 are pending and new.

2. Receipt and consideration of Applicants remarks filed on September 5, 2008 is acknowledged.

3. Rejections not reiterated from the previous Office Action are hereby withdraw~ The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 112, 1st

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. **Claims 39-40 and 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for alleviating acute pain, does not reasonably provide enablement for alleviating <u>any and all pain</u>. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.**

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re*

Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: 1) scope or breadth of the claims; 2) nature of the invention; 3) relative level of skill possessed by one of ordinary skill in the art; 4) state of, or the amount of knowledge in, the prior art; 5) level or degree of predictability, or a lack thereof, in the art; 6) amount of guidance or direction provided by the inventor; 7) presence or absence of working examples; and 8) quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the Examiner's position that one skilled in the art could not practice the invention without undue experimentation.

Scope or breadth of the claims

The scope of the claims is drawn to alleviating any type of pain in a mammal by administering a compound of formula I.

Nature of the invention

The nature of the invention is directed to a method of alleviating any type of pain in a mammal by administering a compound of formula I.

State of, or the amount of knowledge in, the prior art

The art teaches that pain is described an unpleasant sensation that can range from mild localized discomfort to agony. Pain may be contained to a discrete area, as in an injury, or it can be more diffuse, as in disorders like fibromyalgia (see definition of

pain, MedicineNet). Pain can be acute (i.e. pain that comes on quickly and lasts only a short time), chronic (i.e. pain of long duration), neuropathic (pain resulting from damage to nerves), psychogenic (i.e. pain not due to visible signs of disease or injury), or cancer related (effects of a malignant disease on the body) (see the abstract of Zeller et al., *Acute Pain Treatment*, JAMA, volume 299, 2008). Treatment of pain depends on the origin of the pain, and is commonly associated with tissue injury, inflammation, a surgical procedure, childbirth or a brief disease (see *Acute Pain Treatment* and the first paragraph of Drakontides, *Drugs to Treat Pain*). Initial treatments can include non-steroidal anti-inflammatory drugs, opioids (analgesics), muscle relaxants, anesthetics, anticonvulsants, antidepressants, etc. (see the Treatment of pain in Acute Pain Treatment). For example, nitroglycerin can be used in angina and colchicine in gouty arthritis (see the first paragraph in Drakontides, *Drugs to Treat Pain*).

Opioids analgesics in the treatment of neuropathic pain has been controversial in the past, since several studies suggested that opioid therapies are active against certain forms of neuropathic pain (see page 655, column 2 of Ossipov et al., Challenges in the Development of Novel Treatment Strategies for neuropathic pain, The Journal of the American Society for Experimental NeuroTherapeutics, 2(4), 650-661, 2005).

The choice of analgesic is based on the cause, intensity, and probable duration of pain. Successful analgesia depends on knowing the patient and knowing the pharmacological actions, side effects, dependency potential and interactions with other drugs of every medication administered (see the abstract, Drugs to Treat Pain).

Level or degree of predictability, or a lack thereof, in the art

Applicant broadly claims "A method of alleviating pain in a mammal", by administering compounds said to have analgesic activity. Applicant further claims wherein the instant compounds are used to treat different types of pain (i.e. acute, visceral, chronic, and neuropathic).

It is known in the art that pain can be of various types and can be treated with different drugs or classes of drugs depending on various factors, such as, cause, intensity, origin, mechanism of action, duration, etc. (see *Acute Pain Treatment* and the first paragraph of Drakontides, *Drugs to Treat Pain*). Furthermore, with opioid analgesics, there is uncertainty as to whether they will help or act against certain forms of pain. Therefore, it cannot be established that analgesics are capable of treating pain of any kind. The specification provides evidence that the instant compounds have analgesic activity through use of the, tail flick test, which is used to test the acute nocioception of the tail of a mouse or rat (see page 31 of the instant specification and Bannon et al, Models of Nocioception: Hot-plate, tail-Flick, and Formalin tests in Rodents, Current Protocols in Neuroscience, 8.9.1-8.9.16, 2007). However, there is no guidance or data to support that the instant compounds will function to alleviate all types of pain. Thus, there is a high level of unpredictability as to whether the instant compounds will function to alleviate any and all pain.

Amount of guidance or direction provided by the inventor

The specification does not provide any guidance as to how to alleviate all types of pain is said mammal.

Presence or absence of working examples

The specification provides 21 Examples. Twenty of the examples are drawn to the preparation of the instant compounds. One example on page 31 (Example 3) of the specification is drawn to a tail flick test. The analgesic activity of various compounds of formula I are investigated in the tail flick test on the mouse. The compounds showed analgesic action/

Quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure

One of ordinary skill in the art would have to conduct a myriad of experimentation to determine which compounds are effective at alleviating all types of pain. There is no one compound known to treat all types of pain, and opioid analgesics are known to act against certain forms of pain. As a result, one of ordinary skill in the art would be required to conduct an undue amount of experimentation.

For the foregoing reasons, Applicant is not enabled for alleviating all types of pain in a mammal.

6. **Claim 41-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter**

which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: 1) scope or breadth of the claims; 2) nature of the invention; 3) relative level of skill possessed by one of ordinary skill in the art; 4) state of, or the amount of knowledge in, the prior art; 5) level or degree of predictability, or a lack thereof, in the art; 6) amount of guidance or direction provided by the inventor; 7) presence or absence of working examples; and 8) quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the Examiner's position that one skilled in the art could not practice the invention without undue experimentation.

Scope or breadth of the claims

The scope of the claims is drawn to treating or inhibiting anxiety states, stress and stress- associated syndromes, depression, epilepsy, Alzheimer's disease, senile dementia, general cognitive dysfunctions, learning and memory difficulties, withdrawal symptoms, alcohol abuse or dependency, drug abuse or dependency, sexual dysfunction, cardiovascular disease, hypotension, hypertension, tinnitus, pruritus, migraine, impaired hearing, deficient intestinal motility, impaired food intake, anorexia,

obesity, locomotor disorders, diarrhea, cachexia or urinary incontinence in a mammal, said method comprising administering to said mammal an effective amount of a compound according to claim 1 or coadministering to said mammal an effective amount of a compound according to claim 1 with an opioid analgesic or with an anesthetic.

Nature of the invention

The nature of the invention is directed to a method of treating or inhibiting anxiety states, stress and stress- associated syndromes, depression, epilepsy, Alzheimer's disease, senile dementia, general cognitive dysfunctions, learning and memory difficulties, withdrawal symptoms, alcohol abuse or dependency, drug abuse or dependency, sexual dysfunction, cardiovascular disease, hypotension, hypertension, tinnitus, pruritus, migraine, impaired hearing, deficient intestinal motility, impaired food intake, anorexia, obesity, locomotor disorders, diarrhea, cachexia or urinary incontinence in a mammal, said method comprising administering to said mammal an effective amount of a compound according to claim 1 or coadministering to said mammal an effective amount of a compound according to claim 1 with an opioid analgesic or with an anesthetic.

State of, or the amount of knowledge in, the prior art

The art teaches that there are no cures for diseases such as Alzheimer's (AD), dementia, or epilepsy but rather methods of relieving the symptoms of the disease (see the abstract, Griffiths et al., Emerging and potential therapies for Alzheimer's disease,

Expert Opinion of Therapeutic Targets, 12(6): 693-704, 2008, and the abstract, Velisek et al., New avenue of research: antieliptic drug and estradiol neuroprotection in epilepsy, 3(2), 2008). Current and emerging therapies in the treatment of the symptoms of AD include acetylcholinesterase inhibitors, NSAIDs, muscarinic, serotonin and glutamate agonist, estrogens and testosterone (Griffiths et al., Emerging and potential therapies for Alzheimer's disease, Expert Opinion of Therapeutic Targets, 12(6): pg. 694-695, 2008).

Current treatment practices for other diseases or disorders, such as, depression include anti-depressant medication or cognitive therapy (DeRubeis et al. Cognitive therapy versus medication for depression: treatment outcomes and neural mechanism, Nature Reviews, Volume 9, pp 788, 2008). Treatment of pulmonary hypertension includes calcium channel blockers, prostanoids, endothelin receptor antagonists, and phosphodiesterase inhibitors (pg 65 and 68-71 of Driscoll et al, Medical therapy for pulmonary arterial hypertension, Expert Opinion on Pharmacotherapy, 9(1), 2008). Current treatment options surrounding anorexia nervosa have been considered ineffective and more effective test methods need to be performed (Zandian et al., Cause and treatment of anorexia nervosa, Physiology & Behavior, 92 pg 283-290, 2007).

Level or degree of predictability, or a lack thereof, in the art

Applicant broadly claims "A method of treating or inhibiting anxiety states, stress and stress- associated syndromes, depression, epilepsy, Alzheimer's disease, senile dementia, general cognitive dysfunctions, learning and memory difficulties,

withdrawal symptoms, alcohol abuse or dependency, drug abuse or dependency, sexual dysfunction, cardiovascular disease, hypotension, hypertension, tinnitus, pruritus, migraine, impaired hearing, deficient intestinal motility, impaired food intake, anorexia, obesity, locomotor disorders, diarrhea, cachexia or urinary incontinence in a mammal", by administering the instant compounds, said to have analgesic activity.

There are currently no cures for disease such as Alzheimer's, epilepsy, etc. And the treatment options for other diseases or disorders are so divergent, one of ordinary skill in the art cannot be establish whether the instant compounds, which are said to have analgesic action, are capable of treating or inhibiting any of extremely large genus of diseases or disorders recited in the instant claim. The specification provides evidence of analgesic activity of the instant compounds by use of a tail flick test which is used to test the acute nocioception of the tail of a mouse or rat (see page 31 of the instant specification and Bannon et al., Models of Nocioception: Hot-plate, tail-Flick, and Formalin tests in Rodents, Current Protocols in Neuroscience, 8.9.1-8.9.16, 2007). However, the relief of acute pain, which applicant has provided evidence for, does not equate to the treatment or inhibition of the instant diseases or disorders claimed. It is unclear how providing analgesic relief will inhibit or treat diseases or disorders, such as, obesity, depression, cardiovascular disease, etc., or diseases where there are no cure. Especially since pain relief is not required for the treatment of diseases or disorders instantly claimed, but rather used in treating, pain, a symptom that may be associated with some of the diseases or disorders instantly claimed (see the first paragraph in Drakontides, *Drugs to Treat Pain*). There is no guidance or data to support that the

instant compounds will function to inhibit or treat any of the diseases or disorders that applicant has purported. Thus, there is a high level of unpredictability as to whether the instant compounds will treat or inhibit any of the instantly claimed diseases or disorders.

Amount of guidance or direction provided by the inventor

The specification does not provide any guidance as to how to treat or inhibit any of the instantly claimed diseases or disorders.

Presence or absence of working examples

The specification provides 21 Examples. Twenty of the examples are drawn to the preparation of the instant compounds. One example on page 31 (Example 3) of the specification is drawn to a tail flick test. The analgesic activity of various compounds of formula I are investigated in the tail flick test on the mouse. The compounds showed analgesic action.

Quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure

One of ordinary skill in the art would have to conduct a myriad of experimentation to determine which compounds are effective at treating or inhibiting any of the instantly claimed diseases or disorders. There is no one compound known to treat all of those extremely different diseases or disorders instantly claimed and Applicant has not provided any evidence to support that the instantly claimed compounds, with analgesic

activity, are capable of treating or inhibiting any of the instantly claimed diseases or disorders.

As a result, one of ordinary skill in the art would be required to conduct an undue amount of experimentation.

For the foregoing reasons, Applicant **is not enabled for the treatment or inhibition** of the instantly claimed diseases or disorders.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 42 recites " A method of providing a nootropic, muscle relaxant, anticonvulsive, antitussive, anesthetic, antinatriuresis, or for causing diuresis or anxiolysis, said method comprising the step of administering to a patient in need thereof an effective amount of a compound according to claim 1 or coadministering to said mammal an effective amount of a compound according to claim 1 with an opioid analgesic or with an anesthetic."

The claim language is confusing. It is unclear what Applicant intends. It is unclear if Applicant wants to provide a certain effect (e.g. muscle relaxation, diuresis, etc.) to a patient, or if Applicant intends to provide a method for providing a drug to a patient.

Conclusion

7. Claims 1-38 and 43-53 are allowed.

8. Claims 39-42 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KRISTIE L. BROOKS whose telephone number is (571)272-9072. The examiner can normally be reached on M-F 8:30am-6:00pm Est..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KB

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616